

The only solid support taught by Torrence, *et al.*, is controlled pore glass (column 10, lines 49-53), which is not substantially planar. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1-5 Under 35 U.S.C. 103(a)

Claims 1-5 are rejected under 35 U.S.C. 103(a) as being obvious over Torrence, *et al.*, in view of synthesis cycle 10hpaF3 (Reference V) and further in view of Yeung, *et al.* (Anal. Biochem. 18, 66-75 (1990); Reference U). The Examiner states that synthesis cycle 10hpaF3 teaches a cycle in which argon flushing occurs in 100% of the chemical coupling steps. The Examiner states that Yeung, *et al.*, also demonstrates the use of argon flushing. The Examiner states that it would have been obvious for one of ordinary skill in the art to dry the solid support in the method of Torrence, *et al.*, using the cycle functions disclosed by synthesis cycle 10hpaF3 for oligonucleotide synthesis. The Examiner reasons that the increased drying times would improve removal of unwanted components and improve the quality of synthesis of the oligonucleotides. The Examiner further states that Yeung, *et al.*, provides evidence that optimization of elements such as drying time was routine in the art and that an argon drying step of over 60 seconds was known.

Claims 1-5, as amended, are not obvious in light of Torrence, *et al.*, in view of synthesis cycle 10hpaF3 and in view of Yeung, *et al.* Neither synthesis cycle 10hpaF3 or Yeung, *et al.*, teach solid supports that are substantially planar or that have substantially planar regions. Yeung, *et al.*, teaches the use of glass flakes (see page 68, lines 8-11) and synthesis cycle 10hpaF3 is silent regarding any type of support. Therefore, the combined teachings of Torrence, *et al.*, Yeung, *et al.*, and synthesis cycle 10hpaF3 do not teach or suggest all the limitations of the amended claims. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1-17 Under 35 U.S.C. 103(a)

Claims 1-17 are rejected under 35 U.S.C. 103(a) as being obvious over Torrence, *et al.*, in view of synthesis cycle 10hpaF3, further in view of Yeung, *et al.* (Anal. Biochem. 18, 66-75 (1990)), and further in view of McGall, *et al.*, U.S. Patent No. 6,147,205 (Reference A). The Examiner states McGall, *et al.*, teaches a method of nucleic acid synthesis using photoremovable

synthesis and masking. The Examiner concludes that it is obvious to combine McGall, *et al.*, with Torrence, *et al.*, Yeung, *et al.*, and synthesis cycle 10hpaf3, stating that one would be motivated to optimize the method of McGall, *et al.*, to minimize the interfering effects of mixed components upon the synthesis reaction.

MPEP § 2142 states that when making a case of *prima facie* obviousness, three criteria must be met: 1) a suggestion or motivation to modify a reference or combine reference teachings, 2) a reasonable expectation of success and 3) the combined prior art reference must teach or suggest all the claim limitations. As discussed above, the combination of Torrence, *et al.*, Yeung *et al.*, and synthesis cycle 10hpaf3 do not teach or suggest all the limitations of the instant claims, as they provide no teaching or suggestion of substantially planar solid supports. McGall, *et al.*, teaches that solid supports can be flat (column 15, lines 14-15). However, McGall, *et al.*, clearly teaches away from the use of planar solid supports. The solid supports of McGall, *et al.*, are disclosed to be preferably spherical (see column 14, lines 43-44). Thus, a fair reading of the reference would not suggest the preparation of a nucleic acid array on a solid support that is *substantially planar or has substantially planar regions*, as recited in Claims 1-17, as amended.

MPEP § 2141 states that when applying 35 U.S.C. § 103, the four basic tenets of the *Graham* test must be adhered to, including considering the claimed invention as a whole. Case law cited in MPEP § 2141.02 provides further instruction on considering the invention as a whole:

“[A] patentable invention may lie in the discovery of the source of a problem even though the remedy may be obvious once the source of the problem is identified. This is part of the ‘subject matter as a whole’ which should always be considered in determining the obviousness of an invention under 35 U.S.C. § 103.” *In re Spinnoble*, F.2d 578, 585, 160 USPQ 237, 243 (CCPA 1969).

The present application teaches at page 22, lines 5-6, that pitting of a planar substrate was discovered to be a probe synthesis phenomenon occurring during the chemical addition steps and that the pitting was a cumulative process occurring during these chemical addition steps (page 22, lines 29-33). A series of experiments was conducted to determine the source of the pitting (see, for example, page 22, line 3 to page 24, line 24). It was found that increasing the time that a planar substrate was dried with argon reduced the amount of pitting of the substrate (page 23,

lines 11-22). None of the cited references recognized that pitting occurred on planar substrates, and furthermore, none of the cited references teach or suggest a cause or a solution for the pitting of planar substrates. Thus, in considering the invention as a whole, the present invention differs from the prior art in identifying that pitting of a planar substrate results from cumulative chemical coupling steps and solving the problem of pitting by increasing the time that a planar substrate is dried with argon.

Applicants have shown that there is no motivation to combine the teachings of McGall, *et al.*, with that of the other cited references, so that the criteria for making a *prima facie* case of obviousness are not fulfilled for Claims 1-17, as amended. Furthermore, Applicants have discovered that pitting occurs on planar substrate as a result of a synthetic process, and have found a means of solving the problem. Neither the problem nor the solution have been recognized in the cited references. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned at (978) 341-0036.

Respectfully submitted,

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MARKED UP VERSION OF AMENDMENTSClaim Amendments Under 37 C.F.R. § 1.121(c)(1)(ii)

1. (Amended) A method of preparing a nucleic acid array on a solid support, wherein said solid support is substantially planar or comprises substantially planar regions, said method comprising:
 - a) attaching a plurality of nucleic acids to said support to form an array; and
 - b) drying said array by exposing to a dry atmosphere for a period of at least 30 seconds.